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Cortical Metastatic Lesions of the Appendicular Skeleton From Tumors of Known Primary Origin

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Background and Objectives: Metastatic disease represents the most common neoplastic process involving bone. Recently, a small subset of cortical based metastatic lesions has been identified. We attempted to delineate the incidence, origin, location, and possible significance of these lesions within an orthopaedic patient population.

Methods: A chart and radiographic review of patients treated for metastatic disease to bone over a 17-year period was performed. Inclusion criteria for lesions were as follows: 1) an appendicular skeletal site, 2) histopathologic confirmation of origin, and 3) presence within a patient diagnosed with a single, known neoplastic process. The lesions were classified as either cortical or medullary based.

Results: Eighty-three lesions (70 patients) satisfied inclusion criteria. Most lesions were of pulmonary (26), breast (22), renal (16), or prostatic (8) tumor origin. Eighteen lesions (22%) from 15 patients were identified as cortical and represented initial presentation in 7 patients. These lesions were of pulmonary (11), renal (5), and breast (2) tumor origin.

Conclusions: Cortical based metastases within the appendicular skeleton may occur more frequently than previously expected. While tumors of pulmonary and renal origin accounted for 42 of the 83 (51%) appendicular lesions, they were responsible for 16 of the 18 (89%) cortical metastases. This preponderance of pulmonary and renal metastases to the cortex is consistent with previously published reports. Our findings may be of value when diagnosing and treating patients whose initial presentation is a cortically based lesion. *J. Surg. Oncol. 1998;67:255–260.* © 1998 Wiley-Liss, Inc.

KEY WORDS: neoplasm metastasis; bone; lung neoplasms; kidney neoplasms

INTRODUCTION

The most common neoplastic process involving bone is metastatic disease [1] which predominantly involves areas of red marrow such as the skull, axial skeleton, or medullary portion of the appendicular skeleton [2]. Recently, a relatively rare subset of cortically based metastatic lesions, predominantly within the appendicular

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TABLE I. Distribution Among Four Patterns of Cortical Bone Destruction (18 Lesions)*

Type I	Small focal lesions, marginal cortical destruction (2 lesions)
Type II	Large osteolytic cortical destruction (1 lesion)
Type III	Saucerized intracortical destruction with well-defined periosteal reaction (6 lesions)
Type IV	Predominantly cortical destruction extending into the soft tissues as well as the medullary cavity (9 lesions)

*According to classification of Greenspan and Norman [7].

skeleton, has been described in the radiologic literature [3–10]. In fact, only one non-appendicular site, a single skull lesion, has been cited [4]. The origin of these lesions, however, has been debated; the majority of earlier studies report pulmonary tumors to be chiefly, if not solely, responsible [4–7], whereas more recent studies have suggested that many different types of tumors have the capacity to metastasize to the cortex of bone [8,9].

We sought to define the incidence, origin, location, and patient population of cortical metastatic lesions within the appendicular skeleton and to determine whether the features of this subset differ from those of medullary lesions.

PATIENTS AND METHODS

Clinical records and radiographs were reviewed for 103 consecutive patients (56 males, 47 females) treated for skeletal metastatic disease by the senior surgeon (J.T.M.) over a 17-year period. Patients ranged in age from 10 months to 81 years (average age 54 years) and had a variety of diagnosed neoplastic diseases with skeletal metastases, including tumors of pulmonary, renal, breast, prostate, gastrointestinal tract, thyroid, uterine, bladder, neural, and dermal origin. From this patient population, a total of 128 osseous lesions were identified. All cases were then subject to strict clinical, radiographic, and histopathologic criteria.

Clinical Criteria

Patients were excluded if there was any doubt as to the origin of their metastatic lesion(s), either if diagnosed with multiple tumors or if a primary tumor was never identified.

Radiographic Criteria

Metastatic osseous lesions were included if they satisfied three criteria: 1) location within the appendicular skeleton; 2) adequate radiographic evaluation, either with two plain films at perpendicular views to one another or a single plain film complemented with computerized tomography (CT); and 3) location that was either clearly cortical or medullary (including predominantly endosteal erosion). Site and type of bony destruction were recorded.

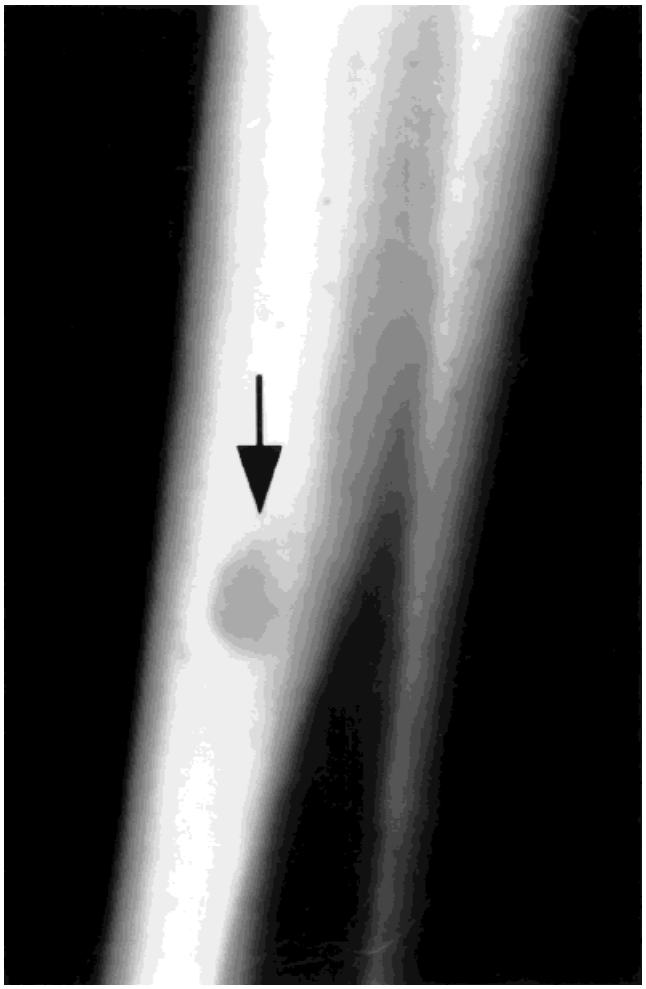

Fig. 1. A sixty-year-old woman with previously diagnosed pulmonary adenocarcinoma who presented with hip pain. Plain films of the femur revealed a small, focal area of cortical destruction (arrow).

Lesions in which osseous destruction was predominantly cortical were categorized according to the classification proposed by Greenspan and Norman [7]. This scheme includes four types of cortical lesions (Table I): type I—small focal lesions or marginal cortical destruction (Fig. 1); type II—large cortical osteolysis (Fig. 2); type III—saucerized intracortical destruction with well-defined periosteal reaction (Figs. 3, 4); and type IV—predominantly cortical destruction extending into soft tissue as well as the medullary cavity (Fig. 5).

Histopathologic Criteria

A specimen from each lesion was obtained either by CT-guided or open biopsy. Each specimen was subject to cytologic and/or histopathologic examination, the results of which were in agreement with an identified primary tumor.

Fig. 2. A sixty-eight-year-old man with an initial presentation of progressive pain in his thigh. Plain films of the femur revealed a large area of osteolytic cortical destruction (arrows). An intramedullary nail was placed as prophylactic fixation. Squamous cell carcinoma of the lung was diagnosed subsequently.

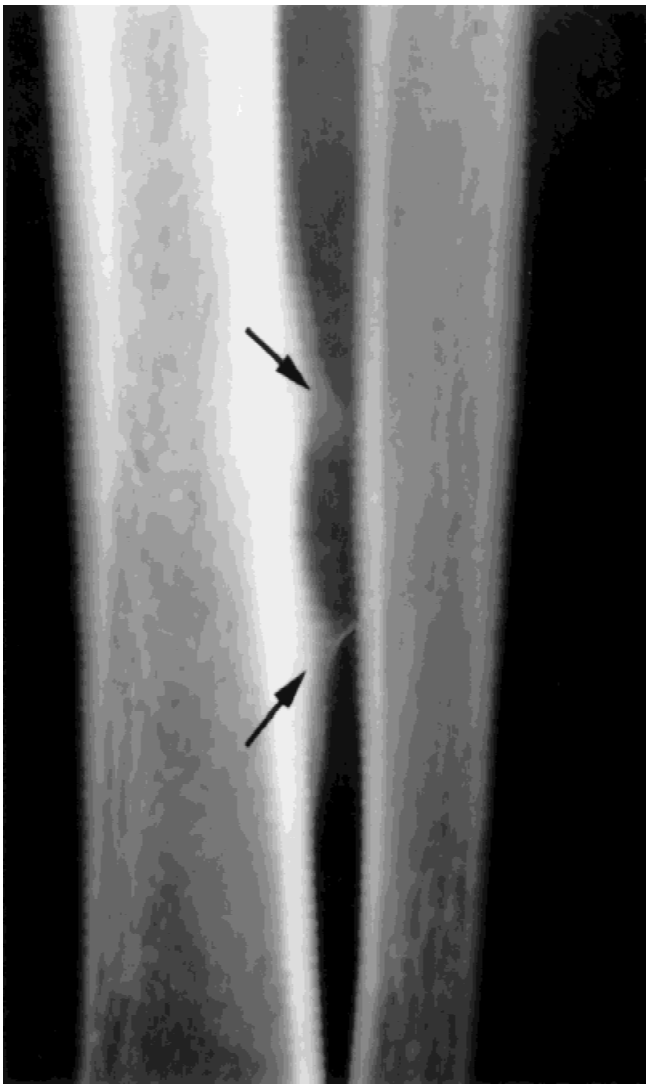

Fig. 3. Fifty-four-year-old man with an initial presentation of progressive pain below his knee. Plain films of the tibia revealed saucerized intracortical destruction with a ring of reactive bone (arrows). Adenocarcinoma of the lung was diagnosed subsequently.

RESULTS

Of the 128 lesions from 103 patients treated over a 17-year period, 83 lesions (70 patients) satisfied the clinical, radiographic, and histopathologic inclusion criteria. Primary neoplastic processes most commonly responsible for this group of metastatic lesions included pulmonary (26), breast (22), renal (16), and prostate (8) (Table II). Twenty-three of 26 lesions in patients with bronchogenic carcinoma were adenocarcinomas. Locations were as follows: femur (51), humerus (22), tibia (7), radius (2), and fibula (1) (Table III).

Eighteen cortical lesions among 15 patients were identified. Patients ranged in age from 51 to 72 years (average age 60 years). Eight of 15 patients were male. Only three primary sites accounted for this group of metastatic lesions, all diagnosed histopathologically following open biopsy: pulmonary (11), renal (5), and breast (2) (Table II). Eight of 11 pulmonary cortical lesions were adenocarcinomas. For 7 of the 15 patients, the cortical lesion was the initial presentation of their malignancy. While the majority of the cortical lesions were located within the femur (10), 4 humeral, 3 tibial, and 1 radial lesion were also identified (Table III).

A chi-square test was used to evaluate the relationship between the site of metastatic lesion and diagnosis of metastasis. Using this method, a positive correlation was established between cortical lesions and pulmonary metastases. *P*-values were two-sided with alpha = 0.05. A 2 × 2 contingency table using pulmonary vs. non-pulmonary metastases and cortical vs. non-cortical lesions was designed and from this a chi score of 9.47 was calculated ($P < 0.01$).

DISCUSSION

A wide array of radiographic diagnostic possibilities must be considered when entertaining the possibility of a metastatic lesion to the cortex. The list includes osteoid

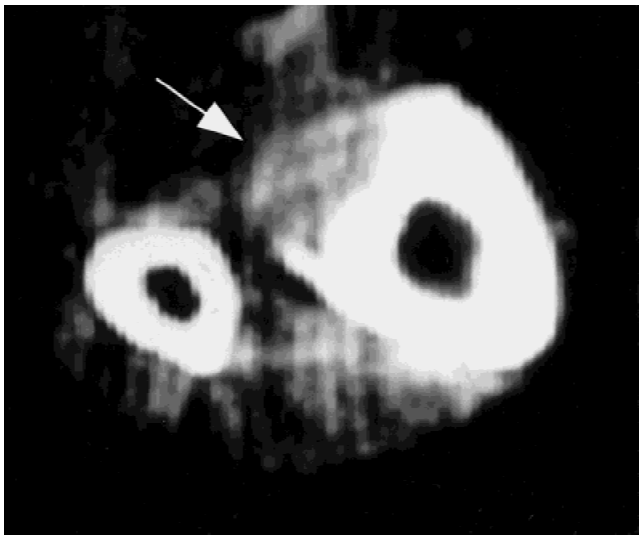

Fig. 4. CT section of lesion in Figure 3 demonstrates cortical destruction with ring of periosteal bone formation (arrow).

TABLE II. Distribution of Tumor Origin

Origin	No. of patients	All bony lesions	Cortical lesions
Pulmonary	22 (31%)	26 (31%)	11 (61%)
Renal	14 (20%)	16 (19%)	5 (28%)
Breast	19 (27%)	22 (27%)	2 (11%)
Prostate	7 (10%)	8 (10%)	0
Other	8 (12%)	11 (13%)	0
Total	70	83	18

osteoma, fibro-osseous dysplasia, intracortical abscess, plasmacytoma, fibrous cortical defect, adamantinoma, Ewing's sarcoma, and hemangioma among many others [11,12]. The documented frequency of skeletal metastases in patients of an appropriate age group with non-osseous primary malignant neoplasms would suggest metastatic disease to be a critical consideration in this differential [1,13,14]. In addition to delineating the relative incidence of cortically based metastases, we wished to uncover any characteristics that may be specific to this group of metastases.

In our study, cortical lesions represented 22% (18 of 83) of all metastatic lesions identified within the appendicular skeleton. While no previous study has attempted to calculate an incidence of metastatic cortical lesions, most suggest that they are exceeding rare [3–6,10]. Since only one previous cortical lesion has been described at a non-appendicular site [4], it is reasonable to assume that limiting our search to the appendicular skeleton may have artificially raised our observed incidence of cortical metastases. Nevertheless, the rate we observed would appear to far exceed that of previous reports. Cortical metastases may not be such a rare event.

Within our patient population we found cortical metastases in patients with three types of primary malignancies. While some were renal (5/18, 28%) and breast carcinoma (2/18, 11%), the majority were pulmonary (11/18, 61%). This preponderance of pulmonary tumors is consistent with previous studies [4–9]. While pulmonary tumors represent the most common malignancy to metastasize to bone, they accounted for a significantly greater proportion of cortical based metastases. The combination of pulmonary and renal tumors comprised approximately one half (42 of 83) of the metastatic lesions to the appendicular skeleton, however, they accounted for almost all (16 of 18) of the cortical based lesions. Previous authors have postulated a possible ''affinity'' of pulmonary tumor cells to cortical bone [8,9]. Mecha-

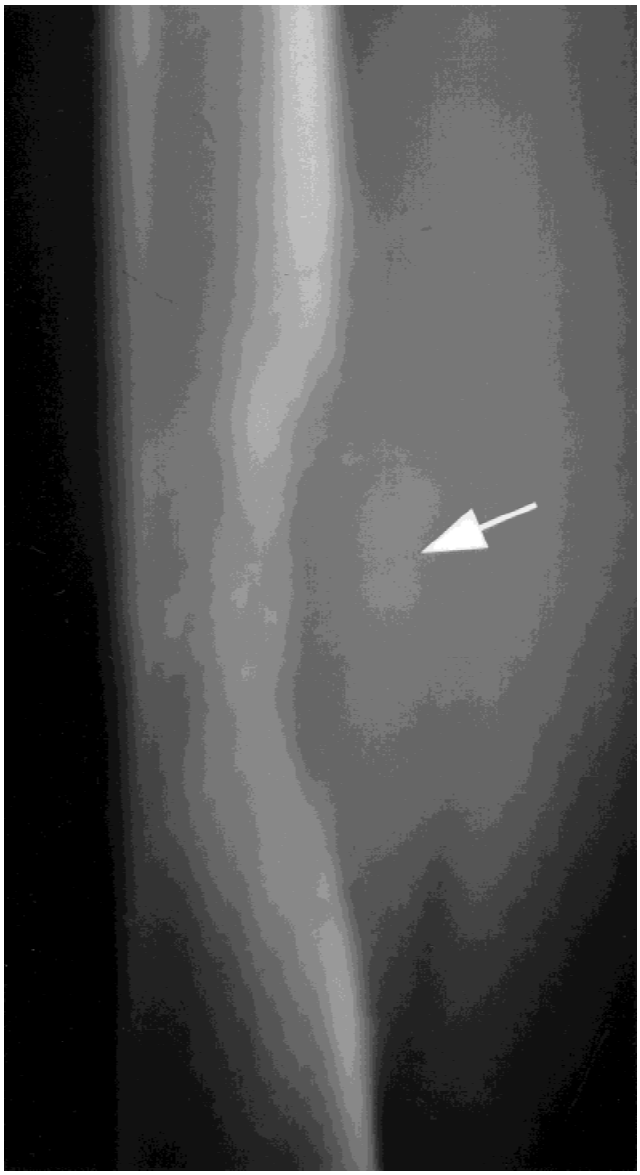

Fig. 5. Fifty-eight-year-old man with previously diagnosed pulmonary adenocarcinoma who developed thigh pain. Plain films of the femur revealed extensive cortical destruction with some extension into the medullary cavity (arrow).

TABLE III. Distribution of Osseous Lesions Within the Appendicular Skeleton

Lesion location	All lesions	Cortical lesions
Femur	51 (62%)	10 (55%)
Tibia	7 (8%)	3 (17%)
Humerus	22 (27%)	4 (22%)
Radius	2 (2%)	1 (6%)
Fibula	1 (1%)	0
Total	83	18

nisms proposed to account for the affinity to tumor cells to bone include altered expression of cell adhesion molecules [15–17] and response to chemoattractants in bone [17–19]. Our data would further support the argument of pulmonary tumor ''affinity'' for bone.

What is perhaps of more significance, however, is the prevalence of adenocarcinoma among pulmonary tumors found to metastasize to bone. Twenty-six metastatic bone lesions (11 of which were cortical) were identified in 24 patients with pulmonary tumors. Twenty-one of the 24 patients were diagnosed with adenocarcinoma of the lung. Adenocarcinoma is only one of a number of bronchogenic tumors, constituting approximately 25–40% of all pulmonary malignancies [20–23]. We found a disproportionately higher incidence of adenocarcinoma among metastatic lesions to bone. The strong association of this histopathologic subtype with skeletal metastases suggests that the previously postulated ''cellular affinity'' of pulmonary tumors may also be specific to subtypes of pulmonary tumors. Several previous studies investigating cortical metastases fail to specify the histopathologic subtype, therefore, limiting an accurate assessment of the incidence of adenocarcinoma within this subset of patients. However, when the histopathologic subtype was included, adeno- and squamous cell carcinomas comprised the majority of bronchogenic tumors metastatic to cortical bone. These intriguing observations are currently the focus of additional study at our institution.

The femur was by far the most common site of bony metastasis (51/83, 62%). The tendency of tumors to metastasize to the femur has been postulated to be of possible significance in the past [8]. Some authors have felt lesion location to be directly related to location and volume of blood flow to a particular bone [9]. In our study, we found the femur to be the most common site of metastatic disease not only among cortical lesions, but also among all metastatic lesions. This predominance may only be a reflection of the relative size and blood flow of the femur. Trias and Fery [24] have demonstrated a distinctly different blood supply to the periosteum and outer cortex. It has been postulated that this anastomotic vascular system may serve as a separate pathway so that metastatic deposits reach compact bone first, destroying cortex [5,24].

Although establishing rigid criteria helped define the study population and aided in evaluating the data, it also provided this study with some limitations. First, our population consisted of patients who had been referred to an orthopaedic surgeon for treatment of skeletal metastatic disease. It is possible that this particular population may not be an accurate reflection of all patients who suffer from skeletal metastatic disease. Perhaps lesions to weight-bearing bones may be more quickly referred, accounting for the very high incidence of femoral lesions. Perhaps renal and pulmonary metastatic lesions comprise a more aggressive subset of lesions that lead to more noticeable radiographic findings and, ultimately, to a greater frequency of referral. Second, our study was limited to the number of lesions found within 70 patients. Obviously this number of patients was sufficient to identify a significant number of cortical metastatic lesions, but it may not be sufficient to establish an accurate rate of metastases to the cortex. Further study with a greater number and variety of patients may help clarify these issues.

Cortical lesions may be of more than academic interest to a physician treating patients with metastatic disease. Such lesions represent a serious threat to the structural integrity of a long bone. This radiographic finding may be indicative of a greater loss of strength of the bone and a higher risk of fracture. The cortical location of a lesion may also serve as a diagnostic aid in patients whose initial presentation may consist of pain and an abnormal radiograph. Seven of our 15 patients identified with a cortical lesion presented in such a manner. Metastatic disease is a critical part of the differential diagnosis of osteolytic lesions of the cortex, and tumors of pulmonary and renal origin must be strongly considered.

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